Case Report

Vitamin B12 and folic acid deficiency presenting as acute febrile illness: a case report

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ABSTRACT

Megaloblastic anemia is not uncommon in India, but data is insufficient regarding its presentation as pyrexia. We report the case of a patient who presented with pyrexia and anaemia, which after exclusion of infective, inflammatory or endocrine causes was attributed to megaloblastic anaemia secondary to vitamin B12 and folic acid deficiency. The patient’s fever responded to treatment of vitamin B12 and folic acid deficiency.

Keywords: Pyrexia, Megaloblastic anemia, Vitamin B12, Folic acid, Pancytopenia

INTRODUCTION

Megaloblastic anemia is a group of disorders characterized by peripheral blood cytopenia which results due to ineffective hematopoiesis in the marrow. They are usually caused by nutritional deficiencies (most common) of either vitamin B12 or folate; or both, inherited disorders of DNA synthesis, or following certain drug therapy.1 Pyrexia in megaloblastic anemia is not an uncommon manifestation. However, megaloblastic anemia secondary to vitamin B12 and folate deficiency, solely as the cause of pyrexia, can be found in only a small proportion of cases, for which differentiation from other causes of fever and fever of unknown origin (FUO) may be difficult even after exhaustive laboratory investigations.2,7,13 Megaloblastic anemia (vitamin B12, folate deficiency) is a reversible cause of pyrexia that should be considered in any patient who presents with pyrexia, macrocytosis and pancytopenia. Usually fever is low grade; however high grade fever may be seen in those patients who present with more severe hematological disease. The proposed underlying mechanism is that megaloblastic anemia causes intramedullary hemolysis and possibly ineffective leucopoiesis and thrombopoiesis. This increased activity in the bone marrow may be related to systemic pyrexia. The aim of this case report was to highlight this aspect of megaloblastic anemia presenting as pyrexia.

CASE REPORT

A 24 year old male, pure vegetarian since birth, presented with easy fatigability for one week and high grade pyrexia (upto 103° F) for the last six days. There was no history of cough, headache, rash, arthralgia, urinary or bowel disturbances. There was no significant past history. Examination of the patient revealed pulse -112/min, BP - 108/60 mm of Hg, temp-102.8°F and marked pallor. There was no icterus, lymphadenopathy, rashes or eschar. There was presence of bald glossy tongue. Cardiovascular system examination revealed tachycardia and ejection systolic murmur in pulmonary area. Abdominal examination showed no organomegaly. Chest and nervous system examination was normal. The profile of complete haemogram at admission is shown in Table 1. Peripheral smear was suggestive of dimorphic anaemia with pancytopenia. There was no parasite in peripheral blood smear, no atypical or immature cells. Quantitative Buffy Coat test for malarial parasites was negative in repeat samples. Biochemical examination was completely...
normal. Urine microscopy, gram stain, Z-N stain and KOH mount was normal. widal test was negative twice. Blood and urine cultures were sterile. Weil felix test was negative. Chest X-ray and ultrasonography of abdomen were normal. Based on low neutrophil count on haematological investigation, patient was managed with broad spectrum antibiotics and empirical antimalarials by artemisinin based combination therapy (ACT). Prothrombin time and INR were normal. Bone marrow examination revealed severe dimorphic anaemia with pancytopenia without presence of any parasite or granuloma, atypical or immature cells. Patient was still febrile. Vitamin B12 level was 137 pg/ml (biological reference interval 211-911 pg/ml) (methodology-Chemiluminescence Immune Assay CLIA) and folate level was 2.96ng/mL (Deficient: 0.35-3.37 ng/mL). Patient’s ANA and CRP levels were normal. Patient was started on injection cyanocobalamin 1000 mcg and 5mg folic acid once daily with ferrous fumarate 1000mg and 5mg daily. Patient was transfused 2 units of B positive packed red blood cells uneventfully.4 days after starting treatment of megaloblastic anaemia, patient was afebrile and remained so thereafter. Patient’s antibiotics were stopped and was discharged after next three days. On follow up after one week, patients haematological examination revealed improvement of anaemia and thrombocytopenia (Table 1).

On follow up patient’s thyroid function tests were done, which were normal.

<table>
<thead>
<tr>
<th>Table 1: Serial hemogram before and after treatment.</th>
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<tbody>
<tr>
<td><strong>Parameter</strong></td>
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<tr>
<td>Hemoglobin (gm%)</td>
</tr>
<tr>
<td>MCV (80-100 fl)</td>
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<tr>
<td>MCH (25-32 pg)</td>
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<tr>
<td>TLC (cells/cumm)</td>
</tr>
<tr>
<td>DLC</td>
</tr>
<tr>
<td>Polymorphs</td>
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<td>Lymphocytes</td>
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<td>Monocytes</td>
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<tr>
<td>Eosinophils</td>
</tr>
<tr>
<td>Platelets (per cumm)</td>
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<tr>
<td>ESR (mm 1st hr)</td>
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<td>Reticulocyte count (%)</td>
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</tbody>
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DISCUSSION

It is shown that fever occurs in about 40% of patients with megaloblastic anemia caused by deficiency of either Vitamin B12 or folic acid or both.69 Usually this is low grade fever and occasionally high grade fever can be seen in those patients with severe anaemia.10,11

Pyrexia is a feature of megaloblastic anaemia that has been described previously in the literature.5,8,11,12 The exact cause of pyrexia in megaloblastic anaemia is not known and probably it may reflect a defect in oxygenation to the thermo-regulatory centres in the brain. However, this theory fails to explain why the fever seen in patients with megaloblastic anaemia is not a recognised feature of other forms of anaemia. Another proposed mechanism is that megaloblastic anaemia leads to hyperplasia and thus increased activity within the bone marrow leading to systemic pyrexia.5,10 The level of pyrexia usually correlates with degree of anaemia and subsides within three days after adequate vitamin supplementation.7,11 this is concordant with our case and this is felt to be due to immediate improvement in ineffective erythropoiesis.5 Patients presenting with fever, anaemia, neutropenia and thrombocytopenia (pancytopenia) are usually treated on the lines of febrile neutropenia with broad spectrum antibiotics and empirical antimalarials, which if caused by megaloblastic anaemia leads to unnecessary antibiotic/antimalarials use and investigations specially in resource poor settings. Patients with anaemia and pyrexia are routinely subjected to complete haemogram with peripheral blood smear examination. Hence patients of pyrexia and features of megaloblastic anaemia or pancytopenia shall be considered for measurement of vitamin B12 and folate levels after ruling out infectious, inflammatory, oncological and endocrine causes. Megaloblastic anaemia, though rare, is a treatable cause of pyrexia.

CONCLUSION

Megaloblastic anaemia is a rare but a known and treatable cause of pyrexia that should be considered in a patient presenting with pyrexia and pancytopenic picture without other infective, inflammatory or endocrine source, who are treated with broad spectrum antibiotics/antimalarials. Measurement of vitamin B12 and folate in such patients and a trial of treatment based on the levels of vitamin B12 and folate, resulting in improvement can avoid the need of further/unnecessary investigations and antibiotic/antimalarial use.

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REFERENCES


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